General

Guideline Title

Myeloma: diagnosis and management.

Bibliographic Source(s)

National Collaborating Centre for Cancer. Myeloma: diagnosis and management. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb 10. 25 p. (NICE guideline; no. 35).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- August 31, 2016 – Opioid pain and cough medicines combined with benzodiazepines : A U.S. Food and Drug Administration (FDA) review has found that the growing combined used of opioid medicines with benzodiazepines or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. FDA is adding Boxed Warnings to the drug labeling of prescription opioid pain and prescription opioid cough medicines and benzodiazepines.
- March 22, 2016 – Opioid pain medicines : The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. They are requiring changes to the labels of all opioid drugs to warn about these risks.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version

of this guidance and related appendices.

Some recommendations are made with more certainty than others. The wording of the recommendations reflects this. For example, the Guideline Committee (GC) uses 'offer' to reflect a strong recommendation, usually where there is clear evidence of benefit. The GC uses 'consider' to reflect a recommendation for which the evidence of benefit is less certain. The strength of recommendation is defined at the end of the "Major Recommendations" field.

See the original guideline document for terms used in this guideline.

Communication and Support

Provide information and support to people with myeloma or primary plasma cell leukaemia and their family members or carers (as appropriate), particularly at diagnosis, at the beginning and end of each treatment, at disease progression and at transition to end of life care.

Consider providing the following information in an individualised manner to people with myeloma and their family members or carers (as appropriate):

- The disease process, relapse and remission cycle, and the person's overall prognosis
- The treatment plan, including (if appropriate) the process and the potential benefits, risks and complications of stem cell transplantation
- Symptoms of myeloma and treatment-related side effects (including steroid-related side effects, infection and neuropathy)
- Lifestyle measures to optimise bone health and renal function
- How to identify and report new symptoms (especially pain and spinal cord compression)
- The role of supportive and palliative care
- How to access peer support and patient support groups

Offer prompt psychological assessment and support to people with myeloma at diagnosis and (as appropriate) at the beginning and end of each treatment, at disease progression and at transition to end of life care.

Refer people who are assessed as needing further psychological support to psychological services.

Advise family members or carers (as appropriate) about the range of available local and national support services at diagnosis, at the beginning and end of each treatment, at disease progression and at transition to end of life care.

For guidance on communication and patient-centred care see the NICE guideline on patient experience in adult NHS services .

Laboratory Investigations

Laboratory Investigations for People with Suspected Myeloma

Use serum protein electrophoresis and serum-free light-chain assay to confirm the presence of a paraprotein indicating possible myeloma or monoclonal gammopathy of undetermined significance (MGUS).

If serum protein electrophoresis is abnormal, use serum immunofixation to confirm the presence of a paraprotein indicating possible myeloma or MGUS.

Do not use serum protein electrophoresis, serum immunofixation, serum-free light-chain assay or urine electrophoresis (urine Bence–Jones protein assessment) alone to exclude a diagnosis of myeloma.

When performing a bone marrow aspirate and trephine biopsy to confirm a diagnosis of myeloma, use morphology to determine plasma cell percentage and flow cytometry to determine plasma cell phenotype.

For guidance on the setup of laboratory diagnostic services see the NICE cancer service guidance on improving outcomes in haematological cancers .

Laboratory Investigations to Provide Prognostic Information

Use the same sample for all diagnostic and prognostic tests on bone marrow, so people only have to have one bone marrow aspirate and trephine biopsy.

When performing a bone marrow aspirate and trephine biopsy to provide prognostic information:

- Perform fluorescence in-situ hybridisation (FISH) on CD138-selected bone marrow plasma cells to identify the adverse risk abnormalities t(4;14), t(14;16), 1q gain, del(1p) and del(17p)(TP53 deletion). Use these abnormalities alongside International Staging System (ISS) scores to identify people with high-risk myeloma.
- Consider performing FISH on CD138-selected bone marrow plasma cells to identify the adverse risk abnormality t(14;20), and the standard risk abnormalities t(11;14) and hyperdiploidy.
- Consider performing immunophenotyping of bone marrow to identify plasma cell phenotype, and to inform subsequent monitoring.
- Consider performing immunohistochemistry (including Ki-67 staining and p53 expression) on the trephine biopsy to identify plasma cell phenotype and give an indication of cell proliferation, to provide further prognostic information.

Perform serum-free light-chain assay and use serum-free light-chain ratio to assess prognosis.

Imaging Investigations

Imaging for People with Suspected Myeloma

Offer imaging to all people with a plasma cell disorder suspected to be myeloma.

Consider whole-body magnetic resonance imaging (MRI) as first-line imaging.

Consider whole-body low-dose computed tomography (CT) as first-line imaging if whole-body MRI is unsuitable or the person declines it.

Only consider skeletal survey as first-line imaging if whole-body MRI and whole-body low-dose CT are unsuitable or the person declines them.

Do not use isotope bone scans to identify myeloma-related bone disease in people with a plasma cell disorder suspected to be myeloma.

Imaging for People with Newly Diagnosed Myeloma

For people with newly diagnosed myeloma or smouldering myeloma who have not had whole-body imaging with one of the following, consider whole-body imaging to assess for myeloma-related bone disease and extra-medullary plasmacytomas with one of:

- MRI
- CT
- Fluorodeoxyglucose positron emission tomography CT (FDG PET-CT).

For guidance on imaging for people with suspected spinal cord compression, see the NGC summary of the NICE guideline Metastatic spinal cord compression. Diagnosis and management of adults at risk of and with metastatic spinal cord compression.

Consider baseline whole-body imaging with MRI or FDG PET-CT for people who have non-secretory myeloma or suspected or confirmed soft tissue plasmacytomas and have not already had either of these tests.

Service Organisation

For guidance on the facilities needed to provide intensive inpatient chemotherapy and transplants for people with myeloma, and the structure and function of multidisciplinary teams (MDTs), see the NICE cancer service guidance on improving outcomes in haematological cancers .

For guidance on service organisation for young people see the NICE cancer service guidance on improving outcomes in children and young people with cancer .

Each hospital treating people with myeloma who are not receiving intensive inpatient chemotherapy or a transplant should provide local access to:

- An MDT specialising in myeloma
- Supportive and palliative care, supported by:
    - Psychological support services
    - A 24-hour acute oncology and/or haematology helpline
    - Physiotherapy
    - Occupational therapy
    - Dietetics
    - Medical social services
    - Critical care
- Clinical trials via the MDT specialising in myeloma

- Dental services

Each hospital treating people with myeloma should provide regional access through its network to:

- Facilities for intensive inpatient chemotherapy or transplantation
- Renal support
- Spinal disease management
- Specialised pain management
- Therapeutic apheresis
- Radiotherapy
- Restorative dentistry and oral surgery
- Clinical trials, in particular early phase trials

Managing Newly Diagnosed Myeloma

First-line Treatment

NICE has a suite of technology appraisal guidance on myeloma either published or in development. These published technology appraisals cover NICE's position in relation to primary disease treatment, salvage therapy for relapsed myeloma and consolidation/maintenance therapy after primary management. The recommendations in this guideline complement the existing technology appraisals, giving further guidance in addition to the technology appraisals where myeloma-related subgroups are not included.

Bortezomib is recommended as an option within its marketing authorisation, that is, in combination with dexamethasone, or with dexamethasone and thalidomide, for the induction treatment of adults with previously untreated multiple myeloma, who are eligible for high-dose chemotherapy with haematopoietic stem cell transplantation. [This recommendation is from the NGC summary of the NICE guideline Bortezomib for induction therapy in multiple myeloma before high-dose chemotherapy and autologous stem cell transplantation (NICE technology appraisal guidance 311).]

Thalidomide in combination with an alkylating agent and a corticosteroid is recommended as an option for the first-line treatment of multiple myeloma in people for whom high-dose chemotherapy with stem cell transplantation is considered inappropriate. [This recommendation is from Bortezomib and thalidomide for the first-line treatment of multiple myeloma (NICE technology appraisal guidance 228).]

Bortezomib in combination with an alkylating agent and a corticosteroid is recommended as an option for the first-line treatment of multiple myeloma if:

- High-dose chemotherapy with stem cell transplantation is considered inappropriate and
- The person is unable to tolerate or has contraindications to thalidomide [This recommendation is from Bortezomib and thalidomide for the first-line treatment of multiple myeloma (NICE technology appraisal guidance 228).]

First Autologous Stem Cell Transplantation

Consider using frailty and performance status measures that include comorbidities to assess the suitability of people with myeloma for first autologous stem cell transplant.

Do not use age or the level of renal impairment alone to assess the suitability of people with myeloma for first autologous stem cell transplant.

Allogeneic Stem Cell Transplantation

Take into account that only a small number of people with myeloma are suitable for allogeneic stem cell transplantation.

When assessing whether people with myeloma are suitable for an allogeneic stem cell transplant, take into account:

- Whether the person has chemosensitive disease
- How many previous lines of treatment they have had
- Whether a fully human leukocyte antigen (HLA) matched donor is available
- How graft-versus-host disease (GvHD) and other complications may get worse with age
- The risk of higher transplant-related mortality and morbidity, versus the potential for long-term disease-free survival
- Improving outcomes with other newer treatments
- The person's understanding of the procedure and its risks and benefits

Consider allogeneic stem cell transplantation as part of a clinical trial if one is available.

Primary Plasma Cell Leukaemia

Consider bortezomib-based and/or lenalidomide-based combination induction chemotherapy for people with primary plasma cell leukaemia.

Consider high-dose melphalan-based autologous stem cell transplantation for people with primary plasma cell leukaemia if they are suitable.

Managing Acute Renal Disease Caused by Myeloma

Consider immediately starting a bortezomib- and dexamethasone-based combination regimen for people with untreated, newly diagnosed, myeloma-induced acute renal disease.

If a bortezomib-based combination regimen is unsuitable for people with untreated, newly diagnosed, myeloma-induced acute renal disease, consider immediately starting a thalidomide- and dexamethasone-based combination regimen[1].

Do not perform plasma exchange for myeloma-induced acute renal disease.

[1]At the time of publication (February 2016), thalidomide in combination with dexamethasone did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

Preventing and Managing Bone Disease

Preventing Bone Disease

To prevent bone disease, offer people with myeloma:

- Zoledronic acid or
- Disodium pamidronate, if zoledronic acid is contraindicated or not tolerated or
- Sodium clodronate, if zoledronic acid and disodium pamidronate are contraindicated, not tolerated or not suitable

Consider immediately referring people with myeloma for dental assessment and treatment before starting zoledronic acid or disodium pamidronate.

For people who need urgent myeloma treatment, consider referring for dental assessment and treatment as soon as possible after they start treatment.

Managing Non-spinal Bone Disease

Offer people with myeloma and non-spinal bone disease who have not already started bisphosphonates:

- Zoledronic acid or
- Disodium pamidronate, if zoledronic acid is contraindicated or not tolerated or
- Sodium clodronate, if zoledronic acid and disodium pamidronate are contraindicated, not tolerated or not suitable

Assess the risk of fracture (in line with the NGC summary of NICE guideline Osteoporosis: assessing the risk of fragility fractures) in people with myeloma and non-spinal bone disease.

Consider surgical stabilisation followed by radiotherapy for non-spinal bones that have fractured or are at high risk of fractures.

Consider radiotherapy for non-spinal bones that have fractured or are at high risk of fracture if surgical intervention is unsuitable or not immediately needed.

Consider radiotherapy for people with myeloma and non-spinal bone disease who need additional pain relief if:

- Chemotherapy and initial pain management has not led to prompt improvement in pain control
- Chemotherapy is unsuitable and current pain medication is not working

Consider re-treatment with radiotherapy if pain recurs or if there is regrowth of a previously treated lesion.

Consider seeking advice from or referral to specialists in palliative care or pain medicine for people with complex non-spinal bone disease.

Managing Spinal Bone Disease

For guidance on treating metastatic spinal cord compression, see the NGC summary of the NICE guideline Metastatic spinal cord compression. Diagnosis and management of adults at risk of and with metastatic spinal cord compression.

Offer all people with myeloma and spinal bone disease:

- Bisphosphonates as follows, if not already started:
  - Zoledronic acid or
  - Disodium pamidronate, if zoledronic acid is contraindicated or not tolerated or
  - Sodium clodronate, if zoledronic acid and disodium pamidronate are contraindicated, not tolerated or unsuitable
- Systemic pain control, when relevant using the NGC summaries of the NICE guidelines Neuropathic pain - pharmacological management. The pharmacological management of neuropathic pain in adults in non-specialist settings and Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults

Consider the following as adjuncts to other treatments for all people with myeloma and spinal bone disease:

- Interventional pain management
- Bracing

In people with radiological evidence of myeloma-related spinal instability, consider immediate intervention with:

- Spinal surgery, with or without radiotherapy
- Cement augmentation, with or without radiotherapy
- Radiotherapy alone, if spinal intervention is unsuitable or not currently needed

In people with radiological evidence of myeloma-related spinal bone disease without instability, consider:

- Cement augmentation, with or without radiotherapy
- Radiotherapy alone

Preventing and Managing Complications

Preventing Infection

Offer people with myeloma the seasonal influenza vaccination.

Consider extending the pneumococcal vaccination to people with myeloma who are under 65.

Consider intravenous immunoglobulin replacement therapy for people who have hypogammaglobulinaemia and recurrent infections.

Consider continuing aciclovir[2] or equivalent antiviral prophylaxis after treatment with bortezomib or other proteasome inhibitors ends.

Consider aciclovir[2] or equivalent antiviral prophylaxis for people who are taking both immunomodulatory drugs and high-dose steroids.

Consider testing for hepatitis B, hepatitis C and human immunodeficiency virus (HIV) before starting myeloma treatment.

[2]At the time of publication (February 2016), aciclovir did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

Managing Peripheral Neuropathy

For guidance on the pharmacological management of neuropathic pain see the NGC summary of the NICE guidelines Neuropathic pain - pharmacological management. The pharmacological management of neuropathic pain in adults in non-specialist settings.

Explain the symptoms of neuropathy to people with myeloma, and encourage them to tell their clinical team about any new, different or worsening neuropathic symptoms immediately.

If people who are receiving bortezomib develop neuropathic symptoms, consider immediately:

- Switching to subcutaneous injections and/or
- Reducing to weekly doses and/or
- Reducing the dose

Consider reducing the dose if people are taking a drug other than bortezomib and develop neuropathic symptoms.

Temporarily stop neuropathy-inducing myeloma treatments if people develop either of the following:

- Grade 2 neuropathy with pain
- Grade 3 or 4 neuropathy

If neuropathy does not improve despite stopping myeloma treatment and further treatment is needed, consider switching to myeloma treatments less likely to induce neuropathy.

Preventing Thrombosis

For people with myeloma who are starting immunomodulatory drugs, offer thromboprophylaxis with either:

- Low molecular weight heparin (LMWH) at a prophylactic dose, or
- Vitamin K antagonists at a therapeutic dose, to maintain an international normalised ratio (INR) of 2–3

If LMWH or vitamin K antagonists are unsuitable, consider low-dose aspirin[3].

When starting thromboprophylaxis, assess the risk factors, contraindications and practicalities of each prophylactic strategy.

Do not offer fixed low-dose vitamin K antagonists for thromboprophylaxis to people with myeloma who are starting immunomodulatory drugs.

Consider switching thromboprophylaxis to low-dose aspirin for people who:

- Are taking immunomodulatory drugs and
- Have achieved maximum response and
- Have no high risk factors

[3]At the time of publication (February 2016), aspirin did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

Managing Fatigue

If other treatable causes of anaemia have been excluded, consider erythropoietin analogues (adjusted to maintain a steady state of haemoglobin at 110–120 g/litre) to improve fatigue in people with myeloma who have symptomatic anaemia.

Monitoring

Monitor people with smouldering myeloma every 3 months for the first 5 years, and then decide the frequency of further monitoring based on the long-term stability of the disease.

Monitor people who have completed myeloma treatment and recovered at least every 3 months. Take into account any risk factors for progression, such as:

- High-risk FISH
- Impaired renal function
- Disease presentation

Monitoring for myeloma and smouldering myeloma should include:

- Assessment of symptoms related to myeloma and myeloma treatment and
- The following laboratory tests:
    - Full blood count
    - Renal function
    - Bone profile
    - Serum immunoglobulins and serum protein electrophoresis
    - Serum-free light-chain assay, if appropriate

Do not offer people with myeloma or smouldering myeloma routine skeletal surveys for disease monitoring.

Consider symptom-directed imaging for people with myeloma or smouldering myeloma if any new bone symptoms develop.

For people with myeloma and serological relapse or disease progression, consider one of the following (taking into consideration previous imaging tests):

- Whole-body MRI
- Spinal MRI
- FDG PET-CT

For people with smouldering myeloma and disease progression, consider one of the following (taking into consideration previous imaging tests):

- Whole-body MRI
- Whole-body low-dose CT
- Whole-body CT
- Spinal MRI
- FDG PET-CT

Managing Relapsed Myeloma

First Relapse

NICE has a suite of technology appraisal guidance on myeloma either published or in development. These published technology appraisals cover NICE's position in relation to primary disease treatment, salvage therapy for relapsed myeloma and consolidation/maintenance therapy after primary management. The recommendations in this guideline complement the existing technology appraisals, giving further guidance in addition to the technology appraisals where myeloma-related subgroups are not included.

Bortezomib monotherapy is recommended as an option for the treatment of progressive multiple myeloma in people who are at first relapse having received 1 prior therapy and who have undergone, or are unsuitable for, bone marrow transplantation, under the following circumstances:

- The response to bortezomib is measured using serum M protein after a maximum of 4 cycles of treatment, and treatment is continued only in people who have a complete or partial response (that is, reduction in serum M protein of 50% or more or, where serum M protein is not measurable, an appropriate alternative biochemical measure of response), and
- The manufacturer rebates the full cost of bortezomib for people who, after a maximum of 4 cycles of treatment, have less than a partial response (as defined above) [This recommendation is from Bortezomib monotherapy for relapsed multiple myeloma (NICE technology appraisal guidance 129).]

People currently receiving bortezomib monotherapy who do not meet the criteria in recommendation above should have the option to continue therapy until they and their clinicians consider it appropriate to stop. [This recommendation is from Bortezomib monotherapy for relapsed multiple myeloma (NICE technology appraisal guidance 129).]

Second Autologous Stem Cell Transplantation

Offer a second autologous stem cell transplant to people with relapsed myeloma who are suitable and who have:

- Completed re-induction therapy without disease progression and
- Had a response duration of more than 24 months after their first autologous stem cell transplant

Consider a second autologous stem cell transplant for people with relapsed myeloma who are suitable and who have:

- Completed reinduction therapy without disease progression and
- Had a response duration of between 12 and 24 months after their first autologous stem cell transplant

Be aware that people with relapsed myeloma are more likely to be suitable for a second autologous stem cell transplant if they have:

- Had a good response to the first autologous stem cell transplant
- A lower ISS stage
- Not had many prior treatments
- Good overall fitness, based on resilience, frailty and performance status
- No adverse FISH results

Subsequent Therapy

Lenalidomide in combination with dexamethasone is recommended, within its licensed indication, as an option for the treatment of multiple myeloma only in people who have received two or more prior therapies, with the following condition:

- The drug cost of lenalidomide (excluding any related costs) for people who remain on treatment for more than 26 cycles (each of 28 days; normally a period of 2 years) will be met by the manufacturer [This recommendation is from Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy (NICE technology appraisal guidance 171).]

People currently receiving lenalidomide for the treatment of multiple myeloma, but who have not received 2 or more prior therapies, should have the option to continue therapy until they and their clinicians consider it appropriate to stop. [This recommendation is from Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy (NICE technology appraisal guidance 171).]

Pomalidomide, in combination with dexamethasone, is not recommended within its marketing authorisation for treating relapsed and refractory multiple myeloma in adults who have had at least 2 previous treatments, including lenalidomide and bortezomib, and whose disease has progressed on the last therapy. [This recommendation is from Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and bortezomib (NICE technology appraisal guidance 338).]

People whose treatment with pomalidomide was started within the NHS before this guidance was published should be able to continue treatment until they and their NHS clinician consider it appropriate to stop. [This recommendation is from Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and bortezomib (NICE technology appraisal guidance 338).]

Definitions

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Committee (GC) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GC is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GC usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the GC uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GC uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer…') are used when the GC is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Clinical Algorithm(s)

A myeloma algorithm is provided in the full version of the guideline (see the "Availability of Companion Documents" field).

In addition, a National Institute for Health and Care Excellence (NICE) pathway titled "Myeloma Overview" is available from the NICE Web site .

Scope

Disease/Condition(s)

Myeloma

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Treatment

Clinical Specialty

Family Practice

Hematology

Internal Medicine

Oncology

Radiation Oncology

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To provide a guideline on the diagnosis and management of myeloma
- To raise standards nationally while allowing clinical flexibility and defining a common pathway for patients with myeloma at various stages of their illness, and of different ages and levels of fitness

Target Population

Adults (aged 16 years and over)

- Who are referred to secondary care with suspected myeloma
- With newly diagnosed or relapsed myeloma (including high-risk myeloma, including primary plasma cell leukaemia)

Note: This guideline does not cover people who have:

- A solitary plasmacytoma without myeloma
- Amyloid light-chain amyloidosis in the absence of myeloma
- Paraproteins secondary to other conditions

Interventions and Practices Considered

Diagnosis/Evaluation

1. Laboratory investigations for people with suspected myeloma
    - Serum protein electrophoresis and serum-free light-chain assay
    - Serum immunofixation
    - Bone marrow aspirate and trephine biopsy, with morphology and flow cytometry
2. Laboratory investigations for prognostic information
    - Fluorescence in-situ hybridisation (FISH) on CD138-selected bone marrow plasma cells
    - Immunophenotyping of bone marrow to identify plasma cell phenotype
    - Immunohistochemistry (including Ki-67 staining and p53 expression) on the trephine biopsy
    - Serum-free light-chain assay and serum-free light-chain ratio to assess prognosis
3. Imaging investigations for people with suspected myeloma
    - Whole-body magnetic resonance imaging (MRI)
    - Whole-body low-dose computed tomography (CT)
    - Skeletal survey
    - Isotope bone scan (not recommended)
4. Imaging investigations for people with newly diagnosed myeloma or smouldering myeloma
    - MRI
    - CT
    - Fluorodeoxyglucose positron emission tomography CT (FDG PET-CT)

Management/Treatment

1. Communication and support
2. Service organisation
3. Managing newly diagnosed myeloma
    - Bortezomib in combination with dexamethasone, or with dexamethasone and thalidomide
    - Thalidomide in combination with an alkylating agent and a corticosteroid
    - Bortezomib in combination with an alkylating agent and a corticosteroid
    - Autologous stem cell transplantation
    - Allogenic stem cell transplantation
4. Managing primary plasma cell leukaemia
    - Bortezomib-based and/or lenalidomide-based combination induction chemotherapy
    - High-dose melphalan-based autologous stem cell transplantation
5. Managing acute renal disease caused by myeloma
    - Bortezomib- and dexamethasone-based combination regimen
    - Thalidomide- and dexamethasone-based combination regimen
    - Plasma exchange (not recommended)
6. Preventing and managing bone disease
    - Bisphosphonates (zoledronic acid, disodium pamidronate, or sodium clodronate)
    - Dental assessment and treatment
7. Managing non-spinal bone disease
    - Bisphosphonates (zoledronic acid, disodium pamidronate, or sodium clodronate)
    - Assessment of fracture risk
    - Surgical stabilisation
    - Radiotherapy
8. Managing spinal bone disease
    - Bisphosphonates (zoledronic acid, disodium pamidronate, or sodium clodronate)
    - Pain control
    - Spinal surgery, with or without radiotherapy
    - Cement augmentation, with or without radiotherapy
    - Radiotherapy alone
    - Specialist referral
9. Preventing infections
    - Seasonal influenza vaccination
    - Pneumococcal vaccination
    - Intravenous immunoglobulin replacement therapy

    - Aciclovir or equivalent antiviral prophylaxis
    - Testing for hepatitis B, hepatitis C and human immunodeficiency virus (HIV) before starting myeloma treatment
10. Managing peripheral neuropathy
11. Preventing thrombosis
    - Low-molecular-weight heparin (LMWH)
    - Vitamin K antagonist
    - Low-dose aspirin
12. Managing fatigue using erythropoietin analogues
13. Monitoring disease activity
14. Managing relapsed myeloma
    - Bortezomib monotherapy
    - Second autologous stem cell transplant
    - Subsequent therapy (lenalidomide in combination with dexamethasone) (pomalidomide in combination with dexamethasone [not recommended])

Major Outcomes Considered

- Overall survival
- Disease-related morbidity and mortality
- Treatment-related morbidity and mortality
- Progression-free survival
- Time to next treatment
- Treatment response rate
- Renal outcome
- Psychological wellbeing
- Diagnostic accuracy
- Number and length of admissions to hospital after diagnosis
- Health-related quality of life
- Patient-reported outcomes
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

Developing Clinical Evidence-based Questions

Method

From each of the key clinical issues identified in the scope, the Guideline Committee (GC) formulated a clinical question. For clinical questions about interventions, the PICO framework was used. This structured approach divides each question into four components: P – the population (the population under study); I – the interventions (what is being done); C – the comparison (other main treatment options); O – the outcomes (the measures of how effective the interventions have been).

Review of Clinical Literature

Scoping Search

An initial scoping search for published guidelines, systematic reviews, economic evaluations and ongoing research was carried out on the following databases or Web sites: National Health Service (NHS) Evidence, NICE, Cochrane Databases of Systematic Reviews (CDSR), Health Technology Assessment Database (HTA), TRIP (Turning Research into Practice), Scottish Intercollegiate Guidelines Network (SIGN), NHS Economic Evaluations Database (NHS EED), Health Economic Evaluations Database (HEED), Medline and EMBASE.

At the beginning of the development phase, initial scoping searches were carried out to identify any relevant guidelines (local, national or international) produced by other groups or institutions.

Developing the Review Protocol

For each clinical question, the information specialist and researcher (with input from other technical team and GC members) prepared a review protocol. This protocol explains how the review was to be carried out (see Table 1 in the full version of the guideline) in order to develop a plan of how to review the evidence, limit the introduction of bias and for the purposes of reproducibility. All review protocols can be found in the evidence review (see Appendix G).

Searching for the Evidence

In order to answer each question the NCC-C information specialist developed a search strategy to identify relevant published evidence for both clinical and cost-effectiveness. Key words and terms for the search were agreed in collaboration with the GC. When required, the health economist searched for supplementary papers to inform detailed health economic work (see "Incorporating Health Economic Evidence" below).

Search filters, such as those to identify systematic reviews (SRs) and randomised controlled trials (RCTs) were applied to the search strategies when necessary. No language restrictions were applied to the search; however, foreign language papers were not requested or reviewed (unless of particular importance to that question).

The following databases were included in the literature search:

- The Cochrane Library
- Medline and Premedline 1946 onwards
- Excerpta Medica (EMBASE) 1974 onwards
- Web of Science [specifically Science Citation Index Expanded (SCI-Expanded) 1900 onwards and Social Sciences Citation Index (SSCI) 1900 onwards]

Subject specific databases used for certain topics:

- Cumulative Index to Nursing and Allied Health Literature (CINAHL) 1937 onwards
- PsycINFO 1806 onwards
- Amed 1985 onwards

From this list the information specialist sifted and removed any irrelevant material based on the title or abstract before passing to the researcher. All the remaining articles were then stored in a Reference Manager electronic library.

In accordance with the 'NICE guidelines manual' (NICE 2012; see the "Availability of Companion Documents" field) searches were updated and re-run 6 to 8 weeks before the guideline was submitted to NICE for stakeholder consultation, thereby ensuring that the latest relevant published evidence was included in the database. Any evidence published after this date was not included. For the purposes of updating this guideline, 8th June 2015 should be considered the starting point for searching for new evidence.

Further details of the search strategies, including the methodological filters used, are provided in the evidence review (see Appendix G).

Critical Appraisal

Following the literature search one researcher independently scanned the titles and abstracts of every article for each question, and full publications were obtained for any studies considered relevant or where there was insufficient information from the title and abstract to make a decision. When papers were obtained, the researcher applied inclusion/exclusion criteria to select appropriate studies, which were then critically appraised. If results from a study were published as more than one paper, the most recent or complete publication was used.

Incorporating Health Economics Evidence

The aim of providing economic input into the development of the guideline was to inform the GC of potential economic issues relating to myeloma.

Health economics is about improving the health of the population through the efficient use of resources. In addition to assessing clinical effectiveness, it is important to investigate whether health services are being used in a cost effective manner in order to maximise health gain from available resources.

Prioritising Topics for Economic Analysis

After the clinical questions had been defined, and with the help of the health economist, the GC discussed and agreed which of the clinical questions were potential priorities for economic analysis. These economic priorities were chosen on the basis of the following criteria, in broad accordance with the NICE guidelines manual (NICE 2012):

- The overall importance of the recommendation, which may be a function of the number of patients affected and the potential impact on costs and health outcomes per patient
- The current extent of uncertainty over cost effectiveness, and the likelihood that economic analysis will reduce this uncertainty
- The feasibility of building an economic model

A review of the economic literature was conducted at scoping. Where published economic evaluation studies were identified that addressed the economic issues for a clinical question, these are presented alongside the clinical evidence.

For systematic searches of published economic evidence, the following databases were included:

- Medline
- EMBASE
- NHS EED
- HTA
- HEED

Number of Source Documents

Refer to the evidence review (see Appendix G in the full guideline appendices [see the "Availability of Companion Documents" field]) for study flow diagrams that provide detailed information for each guideline review question, including total number of records identified, records screened, records excluded, full text articles assessed for eligibility, articles excluded, and studies included in evidence review.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Quality Element	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

Review of Clinical Literature

Critical Appraisal and Evidence Grading

For each question, data were extracted and recorded in evidence tables and an accompanying evidence summary prepared for the Guideline Committee (GC) (see Appendix G). All evidence was considered carefully by the GC for accuracy and completeness.

Grading of Recommendations Assessment, Development and Evaluation (GRADE)

For interventional questions, studies which matched the inclusion criteria were evaluated and presented using GRADE (NICE 2012; http://gradeworkinggroup.org/). Where possible this included meta-analysis and synthesis of data into a GRADE 'evidence profile'. The evidence profile shows, for each outcome, an overall assessment of both the quality of the evidence as a whole (very low, low, moderate or high) as well as an estimate of the size of effect. A narrative summary (evidence statement) was also prepared.

Each outcome was examined for the quality elements defined in Table 2 in the full version of the guideline and subsequently graded using the quality levels listed in the "Rating Scheme for the Strength of the Evidence" field). The reasons for downgrading or upgrading specific outcomes were explained in footnotes.

All procedures were fully compliant with NICE methodology as detailed in the 'NICE guidelines manual' (see the "Availability of Companion Documents" field). In general, evidence was based on published data only. Study authors were contacted only to resolve any ambiguities, such as unclear presentation of data, or where clarification was needed in order to include or exclude a paper in the evidence review.

For non-interventional questions, for example questions regarding diagnostic test accuracy, a narrative summary of the quality of the evidence was provided. The quality of individual diagnostic accuracy studies was assessed using the Quality Assessment of Diagnostic Studies (QUADAS)-2 tool.

Incorporating Health Economics Evidence

Methods for Reviewing and Appraising Economic Evidence

The aim of reviewing and appraising the existing economic literature is to identify relevant economic evaluations that compare both costs and health consequences of alternative interventions and that are applicable to National Health Service (NHS) practice. Thus studies that only report costs, non-comparative studies of 'cost of illness' studies are generally excluded from the reviews (NICE 2012).

Economic studies identified through a systematic search of the literature are appraised using a methodology checklist designed for economic evaluations (NICE 2012). This checklist is not intended to judge the quality of a study per se, but to determine whether an existing economic evaluation is useful to inform the decision-making of the GC for a specific topic within the guideline. There are two parts of the appraisal process; the first step is to assess applicability (i.e., the relevance of the study to the specific guideline topic and the NICE reference case) (see Table 4 in the full version of the guideline).

In the second step, only those studies deemed directly or partially applicable are further assessed for limitations (i.e., the methodological quality) (see Table 5 in the full version of the guideline).

Where relevant, a summary of the main findings from the systematic search, review and appraisal of economic evidence is presented in an economic evidence profile alongside the clinical evidence.

If high-quality published economic evidence relevant to current NHS practice was identified through the search, the existing literature was reviewed and appraised as described above. However, it is often the case that published economic studies may not be directly relevant to the specific clinical question as defined in the guideline or may not be comprehensive or conclusive enough to inform UK practice. In such cases, for priority topics, consideration was given to undertaking a new economic analysis as part of this guideline.

Economic Modelling

Once the need for a new economic analysis for high priority topics had been agreed by the GC, the health economist investigated the feasibility of developing an economic model. In the development of the analysis, the following general principles were adhered to:

- The GC subgroup was consulted during the construction and interpretation of the analysis
- The analysis was based on the best available clinical evidence from the systematic review
- Assumptions were reported fully and transparently
- Uncertainty was explored through sensitivity analysis
- Costs were calculated from a health services perspective
- Outcomes were reported in terms of quality-adjusted life years

See Appendices A and B for details of the health economic analyses undertaken for this guideline, including:

- The cost-effectiveness of alternate imaging strategies for diagnosis in secondary care of patients with suspected myeloma
- The cost-effectiveness of balloon kyphoplasty and vertebroplasty compared to non-surgical management for the treatment of vertebral collapse in patients with myeloma

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

The Guideline Development Process – Who Develops the Guideline?

Overview

The development of this guideline was based upon methods outlined in the 'NICE guidelines manual' (NICE 2012) (see the "Availability of Companion Documents" field). A team of health professionals, lay representatives and technical experts known as the Guideline Committee (GC) (see Appendix F), with support from the NCC-C staff, undertook the development of this clinical guideline. The basic steps in the process of developing a guideline are listed and discussed below:

- Using the remit, define the scope which sets the inclusion/exclusion criteria of the guideline
- Forming the GC
- Developing clinical questions
- Identifying the health economic priorities
- Developing the review protocols
- Systematically searching for the evidence
- Critically appraising the evidence
- Incorporating health economic evidence
- Distilling and synthesising the evidence and writing recommendations
- Agreeing the recommendations
- Structuring and writing the guideline
- Consultation and validation

The Scope

The scope was drafted by the GC Chair and Lead Clinician and staff at the NCC-C in accordance with processes established by NICE. The purpose of the scope was to:

- Set the boundaries of the development work and provide a clear framework to enable work to stay within the priorities agreed by NICE and the NCC-C
- Inform professionals and the public about the expected content of the guideline
- Provide an overview of the population and healthcare settings the guideline would include and exclude
- Specify the key clinical issues that will be covered by the guideline
- Inform the development of the clinical questions and search strategies

Before the guideline development process started, the draft scope was presented and discussed at a stakeholder workshop. The list of key clinical issues were discussed and revised before the formal consultation process. Further details of the discussion at the stakeholder workshop can be found on the NICE Web site (www.nice.org.uk).

The scope was subject to a four week stakeholder consultation in accordance with NICE processes. The full scope is shown in Appendix E. During the consultation period, the scope was posted on the NICE Web site. Comments were invited from registered stakeholder organisations and NICE staff. The NCC-C and NICE reviewed the scope in light of comments received, and the revised scope was reviewed and signed off by NICE and posted on the NICE Web site.

The Guideline Committee

The myeloma GC was recruited in line with the 'NICE guidelines manual' (NICE 2012). The first step was to appoint a Chair and a Lead Clinician. Advertisements were placed for both posts and shortlisted candidates were interviewed in person prior to being offered the role. The NCC-C Director, GC Chair and Lead Clinician identified a list of specialties that needed to be represented on the GC. Details of the adverts were sent to the main stakeholder organisations, cancer networks and patient organisations/charities (see Appendix F). Individual GC members were selected for telephone interview by the NCC-C Director, GC Chair and Lead Clinician, based on their application forms. The guideline development process was supported by staff from the NCC-C, who undertook the clinical and health economics literature searches, reviewed and presented the evidence to the GC, managed the process and contributed to drafting the guideline.

Guideline Committee Meetings

Thirteen GC meetings were held between 27-28 March 2014 and 5–6 November 2015. During each GC meeting (held over either 1 or 2 days) clinical questions and clinical and economic evidence were reviewed, assessed and recommendations formulated. At each meeting patient/carer and service-user concerns were routinely discussed.

NCC-C project managers divided the GC workload by allocating specific clinical questions, relevant to their area of clinical practice, to small sub-groups of the GC in order to simplify and speed up the guideline development process. These groups considered the evidence, as reviewed by the researcher, and synthesised it into draft recommendations before presenting it to the GC. These recommendations were then discussed and agreed by the GC as a whole. Each clinical question was led by a GC member with expert knowledge of the clinical area (usually one of the healthcare professionals). The GC subgroups often helped refine the clinical questions and the clinical definitions of treatments. They also assisted the NCC-C team in drafting the section of the guideline relevant to their specific topic.

Patient/Carer Members

Individuals with direct experience of myeloma services gave an important user focus to the GC and the guideline development process. The GC included three patient/carer members. They contributed as full GC members to writing the clinical questions, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology relevant to the guideline and bringing service-user research to the attention of the GC.

Expert Advisers

During the development of the guideline the GC identified the management of non-spinal and spinal bone disease as topics that required additional expert input. Four experts were identified by the NCC-C and GC (see Appendix F) and invited to advise the GC on drafting their recommendations for that clinical question.

Agreeing the Recommendations

For each clinical question the GC were presented with a summary of the clinical evidence, and, where appropriate, economic evidence, derived from the studies reviewed and appraised. The GC derived their guideline recommendations from this information. The link between the evidence and the view of the GC in making each recommendation is made explicitly in the accompanying Linking Evidence to Recommendations (LETR) statement (see below).

Wording of the Recommendations

The wording used in the recommendations in this guideline denotes the certainty with which the recommendations were made. Some recommendations were made with more certainty than others. Recommendations are based on the trade-off between the benefits and harms of an intervention, whilst taking into account the quality of the underpinning evidence.

For all recommendations, it is expected that a discussion will take place with the patients about the risks and benefits of the interventions, and their values and preferences. This discussion should help the patient reach a fully informed decision. Terms used within this guideline are:

- 'Offer' – for the vast majority of patients, an intervention will do more good than harm
- 'Do not offer' – the intervention will not be of benefit for most patients
- 'Consider' – the benefit is less certain, and an intervention will do more good than harm for most patients. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for an 'offer' recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

LETR Statements

As clinical guidelines were previously formatted, there was limited scope for expressing how and why a GC made a particular recommendation from the evidence of clinical and cost effectiveness. To make this process more transparent to the reader, NICE have introduced an explicit, easily understood and consistent way of expressing the reasons for making each recommendation. This is known as the 'LETR statement' and will usually cover the following key points:

- The relative value placed on the outcomes considered
- The strength of evidence about benefits and harms for the intervention being considered
- The costs and cost effectiveness of an intervention
- The quality of the evidence
- The degree of consensus within the GC
- Other considerations – for example equalities issues

Where evidence was weak or lacking the GC agreed the final recommendations through informal consensus. Shortly before the consultation period five key research recommendations were selected by the GC for implementation and the patient algorithms were agreed.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Committee (GC) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GC is confident that, given the information it has looked at, most people would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GC usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GC uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of people, an intervention will do more good than harm, and be cost effective. The GC uses similar forms of words (for example, 'Do not offer…') when they are confident that an intervention will not be of benefit for most people.

Interventions That Could Be Used

The GC uses 'consider' when confident that an intervention will do more good than harm for most people, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the person's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the person.

Cost Analysis

Relevant health economic evidence for recommendations can be found in the specific chapters of the full version of the original guideline document (see the "Availability of Companion Documents" field).

See Appendices A and B in the full guideline appendices (see the "Availability of Companion Documents" field) for details of the health economic analyses undertaken for this guideline update, including:

- The cost-effectiveness of alternate imaging strategies for diagnosis in secondary care of patients with suspected myeloma
- The cost-effectiveness of balloon kyphoplasty and vertebroplasty compared to non-surgical management for the treatment of vertebral collapse in patients with myeloma

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Consultation and Validation of the Guideline

The draft of the guideline was prepared by the National Collaborating Centre for Cancer (NCC-C) staff in partnership with the Guideline Committee (GC) Chair and Lead Clinician. This was then discussed and agreed with the GC and subsequently forwarded to the National Institute for Health and Care Excellence (NICE) for consultation with stakeholders.

Registered stakeholders had one opportunity to comment on the draft guideline which was posted on the NICE Web site between 19 August 2015 and 1 October 2015 in line with NICE methodology (NICE 2014 [see the "Availability of Companion Documents" field]).

The Pre-publication Process

An embargoed pre-publication version of the guideline was released to registered stakeholders who have signed a confidentiality form to allow them to see how their comments have contributed to the development of the guideline and to give them time to prepare for publication.

The final document was then submitted to NICE for publication on their Web site. The other versions of the guideline were also discussed and approved by the GC and published at the same time.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type and quality of evidence supporting each review question are described in evidence profiles in the full version of the guideline and Appendix G (see the "Availability of Companion Documents" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of myeloma, including management of complications of treatment

See the "Trade-off between benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for details about benefits of specific interventions.

Potential Harms

- The Guideline Committee (GC) recognised that there may be an increase in referral of people who do not have myeloma (and associated anxiety) resulting from a false-positive test.
- The GC agreed that a potential harm of the use of whole body computed tomography (CT) was radiation exposure. However they minimised this by recommending that magnetic resonance imaging (MRI) should be considered first and CT only if MRI was not suitable.
- Autologous stem cell transplant could potentially be performed in someone who was too frail and there may be an increase in morbidity. However, it was agreed that the biological status of the patient will be the deciding factor in whether they are suitable for transplant.
- The GC noted that the risks of allogeneic stem cell transplantation are known to be significant compared with those of other treatments (e.g., autologous transplant).
- The GC noted that morbidity (toxicity and adverse events) and mortality is associated with many of the recommended treatments.

See the "Trade-off between benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for additional harms of specific interventions.

Qualifying Statements

Qualifying Statements

- The recommendations in this guideline represent the view of the National Institute for Health and Care Excellence (NICE), arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The application of the recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.
- Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

Guideline Implementation

The National Institute for Health and Care Excellence (NICE) invited stakeholders to give their responses to the following questions during consultation of the guideline:

- Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why.
- What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.)

NICE will use the feedback received to inform their support activities for this guideline.

Implementation Tools

Clinical Algorithm

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Collaborating Centre for Cancer. Myeloma: diagnosis and management. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb 10. 25 p. (NICE guideline; no. 35).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Feb 10

Guideline Developer(s)

National Guideline Alliance - National Government Agency [Non-U.S.]

Source(s) of Funding

The National Collaborating Centre for Cancer (NCC-C) was commissioned by the National Institute for Health and Care Excellence (NICE) to develop this guideline.

Guideline Committee

Guideline Committee (GC)

Composition of Group That Authored the Guideline

Guideline Committee (GC) Members: Professor Curly Morris (*Chair*), Consultant Haematologist, Altnagelvin Hospital, Londonderry; Dr Guy Pratt (*Lead Clinician*), Senior lecturer, Cancer Sciences Honorary Consultant Haematologist, Birmingham; Professor Sam Ahmedzai, Emeritus Professor, Palliative Medicine, Sheffield; Alan Chant, Patient and carer member; Andrea Guy, Clinical Nurse Specialist and Stem Cell Transplant Coordinator, Myeloma and Related Plasma Cell Disorders, London; Dr Matthew Jenner, Consultant Haematologist, Southampton; Nicola Montacute, Palliative Care Clinical Nurse Specialist, Somerset; Dr Nicola Mulholland, Consultant Radiologist and nuclear medicine physician, honorary senior lecturer, London; Monica Morris, Clinical Nurse Specialist, Middlesex; Lesley Roberts, Patient and carer member; Dr Hamdi Sati, Consultant Haematologist, Swansea; Professor John Snowden, Consultant Haematologist & Director of Blood and Marrow Transplantation, Sheffield; Dr Matthew Streetly, Consultant Haematologist, London; Jane Woodward, Patient and carer member

Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Committee (GC) members' interests were recorded on a standard declaration form that covered consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GC meetings, members declared new, arising conflicts of interest which were always recorded (see Appendix F in the full guideline appendices [see the "Availability of Companion Documents" field]).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub and eBook formats from the NICE Web site .

Availability of Companion Documents

The following are available:

- Myeloma: diagnosis and management. Full guideline. London (UK): National Institute for Health and Care Excellence; 2016 Feb. 287 p. (NICE guideline; no. 35). Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Myeloma: diagnosis and management. Appendices A-F. London (UK): National Institute for Health and Care Excellence; 2016 Feb. 89 p. (NICE guideline; no. 35). Available from the NICE Web site .
- Myeloma: diagnosis and management. Appendix G: evidence review. London (UK): National Institute for Health and Care Excellence; 2016 Feb. 670 p. (NICE guideline; no. 35). Available from the NICE Web site .
- Myeloma: diagnosis and management. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence; 2016 Feb. (NICE guideline; no. 35). Available from the NICE Web site .
- Myeloma: diagnosis and management. Resource impact report. London (UK): National Institute for Health and Care Excellence; 2016 Feb. 6 p. (NICE guideline; no. 35). Available from the NICE Web site .
- Myeloma: diagnosis and management. Learning podcast. Available from the NICE Web site .
- Myeloma: diagnosis and management. Implementation podcast. Available from the NICE Web site .
- The guidelines manual 2012. London (UK): National Institute for Health and Care Excellence (NICE); 2012 Nov. Available from the NICE Web site .
- Developing NICE guidelines: the manual. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Oct. Available from the NICE Web site .

Patient Resources

The following is available:

- Myeloma: diagnosis and management. Information for the public. London (UK): National Institute for Health and Care Excellence; 2016 Feb. 18 p. (NICE guideline; no. 35). Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in eBook and ePub formats from the NICE Web site .

NGC Status

This NGC summary was completed by ECRI Institute on May 20, 2016. This summary was updated by ECRI Institute on October 21, 2016 following the U.S. Food and Drug Administration advisory on opioid pain and cough medicines combined with benzodiazepines.

The National Institute for Health and Care Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their clinical guidelines with the intention of disseminating and facilitating the implementation of that guidance. NICE has not yet verified this content to confirm that it accurately reflects that original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE clinical guidelines are prepared in relation to the National Health Service in England and Wales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at www.nice.org.uk .

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